

comparison with certain compounds coming within the scope of the present invention.

The first of these declarations, that of Dr. Raymond William Keogh, reports the results of comparative tests of a compound of the present invention in comparison with Yamanouchi's compound for effectiveness in inhibiting an allergic reaction in rats produced by an injection of an antigen to which the rats had previously been sensitized. The effectiveness of the test compound was gauged from the reduction in size of a skin weal due to the allergic reaction in comparison with the size of the weal in control animals. In this manner, the amount of test compound ( $ID_{50}$ ) required to produce a 50% inhibition in the weal size was determined. As shown in the declaration (page 3), the compound of the present invention had an  $ID_{50}$  of 0.02 mg/kg, whereas Yamanouchi's compound had an  $ID_{50}$  of more than 10 mg/kg, thus indicating that the compound of the present invention is more than 500 times as effective in inhibiting the results of the anitgen-antibody reaction.

Also submitted herewith is a declaration of Dr. Dale Michael Jackson which reports the results of comparative tests of the above-identified compound of Yamanouchi in comparison with two compounds coming within the scope of the present invention. The test procedure followed by Dr. Jackson produces results which reflect the anti-allergic activity of the compounds, by measuring the ability of a compound under test to block the action of sodium cromoglycate given as a challenge to a test animal. The results of the test (page 4 of the declaration) showed that compounds A and B, representative of the compounds of the invention were vastly superior in anti-allergic activity to compound C, which is the compound disclosed by Yamanouchi. Whereas both of the compounds (A and B) of the invention were 100% effective in

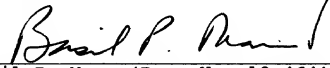
blocking the effect of the challenge dose, the compound (C) of Yamanouchi showed no effectiveness.

It is submitted that the newly presented declarations of Drs. Keogh and Jackson as well as the previously submitted declaration of Dr. Keogh establish by direct comparison testing the unobvious superiority of the compounds of the present invention with respect to the closest compounds of the prior art. Accordingly, the presumption of obviousness which arises from the teachings of the references has been effectively rebutted.

Reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,  
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